SPECIFIC OR UNSPECIFIC ANTIBODIES APPEARING IN THE CEREBROSPINAL FLUID IN SOME EXPERIMENTAL MENINGITIDES

AUTHOR(S):

Sumi, Hiroshi

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From the 1st Surgical Division, Faculty of Medicine,
Kyoto University, (Director ; Prof. CHISATO ARAKI)

by

HIROSHI SUMI.

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Using a serological reaction named volumination* (Torikata), Kato in our laboratory studied on the changes in the amount of antibodies appearing in the cerebrospinal fluid during the course of acute meningitis caused by staphylococcus or bacterium coli for the purpose of evaluating some immunological procedures to be used for the prevention and treatment of posttraumatic meningitis.

However, staphylococcus and bacterium coli appeared to be unsuitable for the experiments, because they do not produce specific antibodies significantly enough to influence on the course of the infection.

In the present work I have made the experiments with tetanus becillus and pneumococcus, the method being otherwise almost similar to those of Kato. Since tetanus bacillus does not affect meninges in its natural infection, these experiments are quite extraordinary ones.

I. Experimental materials.

1) Animals ; 2 rabbits weighing about 2 Kg. were used in pairs in all experiments.

2) Bacterial suspensions used for the infection.

a) Tetanus bacillus ; strain Riku. No. 3 cultured in the T. G. C. solution, given from the Aichi Serum Institute, is suspended in the amount of each 1/60, 1/45 and 1/15 platinum loop in 0.5 cc of physiological saline solution.

b) Pneumococcus ; strain No. 2 cultured on the cystin blood agar, given from the Infectious Diseases Research Institute, is suspended in the amount of 1/400,000, 1/200,000, 1/2,000 and 1/1,000 platinum loop in 0.5 cc of physiological saline solution.

3) Tetanus-anatoxin used for active immunization, and antiserum for treatment of meningitis ; anatoxin containing 20 Test Doses in 1.0 cc and antiserum with the titre of 600 International Antiserum Units in 1.0 cc are used. Both were given from the Aichi Serum Institute.

4) Pneumococcus vaccine for active immunization ; 1.0 mg. of pneumococcus is suspended in 1.0 cc of physiological saline solution and kept at 60 degree C. for 30 minutes.

*Volumination is a reaction, indicated by the increase in the volume of the centrifugate of the bacteria, which has been brought into action with specific or unspecific antibodies in a Torikata's volumetric precipitometer.

5) Licopodium for the production of aseptic meningitis (control); 2 mg. licopodium is suspended in 0.5 cc of phyisiological saline solution and boiled for 30 minutes in an ampulla.

6) Bacterial suspension ; tetanus bacillus and pneumococcus for antigens in the test of volumination are used in saline water suspensions, each 1.0 cc of which gives a precipitate measuring 10 graduations of Torikata's volumetric precipitometer. They are boiled for 30 minutes.

Ⅱ. Method of immunization and volumination.

1) For the animals to be infected with tetanus.

a) 1.0 cc of tetanus-anatoxin was preliminarily injected to the animals subcutaneously 3 times every 4 days. The last injection was done 2 weeks before the experimental tetanal infection.

b) Antiserum was given subcutaneously once a day for 4 days after the infection, decreasing the doses day after day, for instance 1.0, 0.8, 0.6 and 0.4 cc.

2) For the animals to be infected with pneumococcus.

Pneumococcus vaccine was given intracutaneously once a day for 5 days, increasing the doses day after day, for instance 0.1, 0.2, 0.3, 0.4 and 0.5 cc, and the infection was carried out 9 days after the last vaccination.

3) Licopodium or bacterial suspensions were introduced into the meningeal space of rabbits by suboccipital puncture and then about 1.0 cc of the cerebrospinal fluid was taken for examination once a day by the same route.

4) The antibody content of the cerebrospinal fluid was determined by the volumination. Procedures of the volumination are given in the following.

a) The serum or the cerebrospinal fluid taken from the experimental rabbits is centrifuged for the purpose of excluding cellular admixtures and then kept at 56 degree C. for 30 minutes in a water-bath.

b) Each 1.0 cc of the suspension of tetanus bacillus or pneumococcus is introduced into a Torikata's volumetric precipitometer.

c) Each 0.5 cc of the serum or the cerebrospinal fluid aforementioned is added to it.

d) They are mixed thoroughly by a blower and kept at 37 degree C. for 1 hour in an incubator.

e) Then, mixed them again as stated above, they are centrifuged for 30 minutes at 3,000 r. p. m. The bacterial sediment is read in the capillary portion of the precipitometer. One graduation of the precipitometer corresponds to 0.0007 cc.

f) Together with these precipitometer (as they were, antigen-antibody precipitometer) a control precipitometer is treated in just the same way and read, which contains the bacterial suspension and the physiological saline solution in the same amount as the serum or the fluid in the other precipitometers (antigen only precipitometer).

g) The ratio of the reading in the antigen only precipitometer (taken as

1.000) to that in the antigen-antibody precipitometer gives the value of the volumination.

Ⅲ. Changes in the amount of antibodies appearing in the cerebrospinal fluid in tetanus meningitis.

1) In normal rabbits.

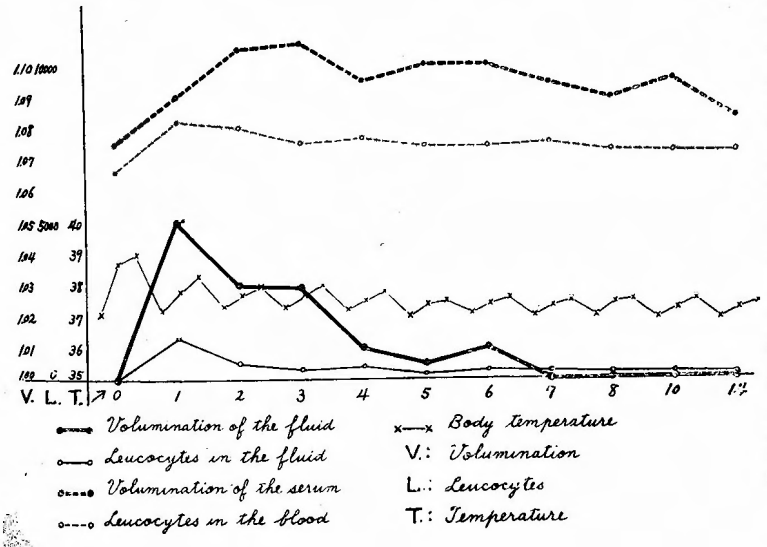
a) There is no trace of antibodies demonstrable by the volumination in the normal cerebrospinal fluid. However, after the injection of 2 mg. of licopodium suspension in 0.5 cc of physiological saline solution into the meningeal space, the antibody against tetanus bacillus appears in the cerebrospinal fluid, reaches the maximal value (1.050) at 24 hours after the injection, then decreases gradually and disappears after 7 days. The ratio of the volumination of the fluid to that of the serum at the highest period of the former is 0.96 and the maximal increase in leucocytes in the fluid is 1,315 after 24 hours (Table & Fig. 1.)

Table 1. Volumination of the fluid agaist tetanus bacillus in case of meningitis due to suboccipital injection of 2 mg licopodium average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0*	22	6600	37.1	38.7	39.0	1.000	1.075	0.93
1	1315	8200	37.2	37.8	38.3	1.050	1.090	0.96
2	500	8000	37.3	37.7	38.0	1.030	1.105	0.93
3	315	7500	37.3	37.7	38.0	1.029	1.107	0.93
4	385	7650	37.2	37.5	37.8	1.010	1.095	0.92
5	160	7400	37.0	37.4	37.5	1.005	1.100	0.91
6	260	7400	37.1	37.4	37.6	1.010	1.100	0.92
7	235	7500	37.0	37.3	37.5	1.000	1.094	0.91
8	190	7250	37.0	37.4	37.5	1.000	1.089	0.92
10	195	7200	36.9	37.2	37.5	1.000	1.095	0.91
14	160	7200	36.9	37.2	37.4	1.000	1.083	0.92

* indicates the time of injection.

Fig. 1.



b) When 1/60 platinum loop of tetanus bacillus suspended in 0.5 cc of physiological saline solution has been introduced into the suboccipital cistern, the appearance of the antibody in the fluid is as follows ; the highest value of the volumination of the fluid is 1.034 and is attained 48 hours after the infection, the antibody being demonstrable for 7 days. The fluid-serum volumination ratio is 0.96 before the infection and 24 - 72 hours, there after and the highest number of leucocytes in the fluid is 785 after 24 hours (Table & Fig. 2.).

c) In case of the in-

jection of 1/45 platinum loop of tetanus bacillus suspended in 0.5 cc of physiological saline solution, the volumination is 1.024 at the highest level 48 and 72 hours after the infection, and disappears completely on the 7th day. The highest fluid-serum volumination ratio is 0.96 after 72 hours and the highest number of leucocytes in the fluid is 480 after 24 hours (Table & Fig. 3.)

Comment.

The maximal value and the duration of the appearance of antibody demonstrable by the volumination in the fluid are almost the same in each of these experiments; i. e. specific antibody does not increase in a particularly larger amount in the fluid by the inoculation of tetanus bacillus into the meningeal space. There is no much difference in the antibody content in the fluid between meningitis due to licopodium and tetanus bacillus. The antibodies in the fluid in these cases seem to be unspecific.

The body temperature of the rabbits does not rise remarkably.

The pleocytosis is

Table 2. Volumination of the fluid against tetanus bacillus in case of meningitis following suboccipital injection of 1/60 platinum loop tetanus bacilli average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	13	7400	37.7	37.9	39.0	1.000	1.045	0.96
1	785	8500	38.1	38.5	38.9	1.004	1.049	0.96
2	380	10900	37.6	37.9	38.3	1.034	1.073	0.96
3	435	8800	37.8	38.0	38.8	1.004	1.043	0.96
4	350	9500	38.2	38.7	38.7	1.019	1.073	0.95
5	285	10150	38.2	38.4	38.8	1.015	1.090	0.93
6	225	8700	38.3	38.6	38.7	1.019	1.084	0.94
7	340	9100	38.2	38.4	38.5	1.000	1.063	0.94
8	310	8500	38.7	38.7	39.1	1.000	1.063	0.94
10	450	8700	37.8	38.4	38.8	1.000	1.054	0.95
11	335	8200	37.9	38.3	38.6	1.000	1.054	0.95

Fig. 2.

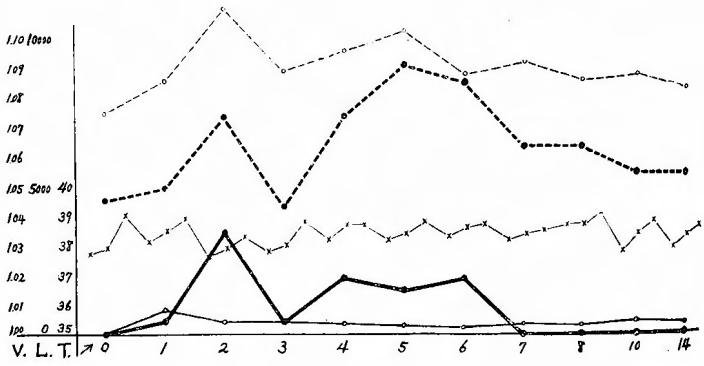


Table 3. Volumination of the fluid against tetanus bacillus in case of intracisternal injection of 1/15 platinum loop tetanus bacilli average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	31	7900	37.0	37.4	38.7	1.000	1.054	0.95
1	180	7500	37.5	37.9	38.1	1.000	1.064	0.94
2	300	8000	37.5	37.9	38.2	1.021	1.078	0.95
3	190	7200	37.3	37.8	38.1	1.024	1.064	0.96
4	255	7200	37.2	37.7	38.1	1.009	1.068	0.94
5	340	6900	37.4	37.7	38.0	1.000	1.081	0.92
6	355	7300	37.3	38.0	38.0	1.004	1.084	0.93
7	355	8750	37.2	37.7	38.0	1.000	1.055	0.95
8	190	7800	37.1	37.6	37.8	1.000	1.061	0.94
10	205	6500	37.2	37.8	38.0	1.000	1.063	0.94
11	105	7700	37.1	37.5	37.8	1.000	1.055	0.95

greater in aseptic meningitis due to licopodium than in tetanal meningitis.

2) Experiments in the rabbits, preliminarily immunized.

Fig. 3.

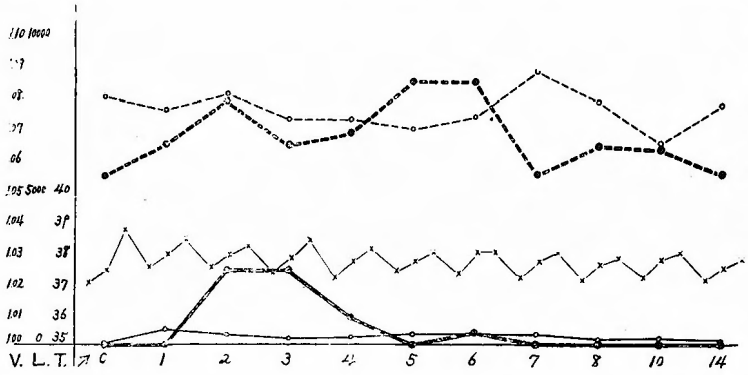
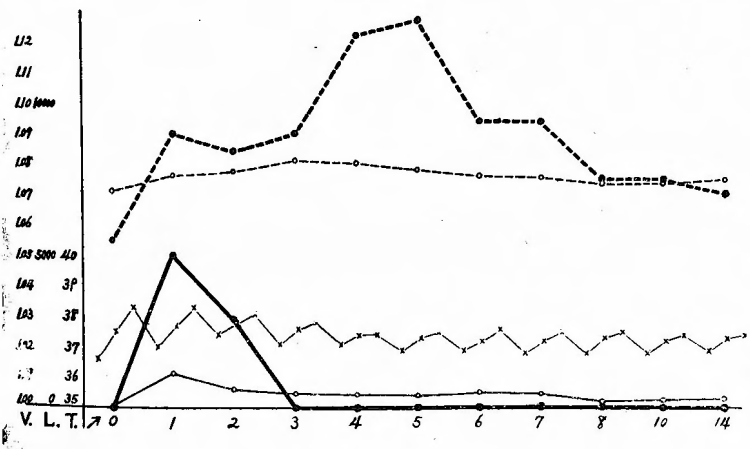


Table 1. Volumination of the fluid against tetanus bacillus in case of intrasicternal injection of 2 mg licopodium after preliminary anatoxin injection average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	35	7100	36.6	37.5	38.3	1.000	1.055	0.95
1	1100	7600	37.0	37.7	38.3	1.050	1.090	0.96
2	595	7750	37.4	37.8	38.1	1.029	1.084	0.95
3	460	8100	37.1	37.6	37.8	1.000	1.090	0.92
4	425	8000	37.1	37.4	37.4	1.000	1.122	0.89
5	375	7800	36.9	37.3	37.5	1.000	1.127	0.89
6	500	7600	36.9	37.2	37.6	1.000	1.094	0.91
7	440	7550	36.8	37.2	37.5	1.000	1.094	0.91
8	220	7300	36.8	37.3	37.5	1.000	1.075	0.93
10	240	7400	36.8	37.2	37.4	1.000	1.075	0.93
14	295	7450	36.9	37.3	37.4	1.000	1.070	0.93

Fig. 4.



a) The rabbits which have been immunized by tetanus-anatoxin, are injected intracisternally with the same dose of licopodium suspension as in the previous experiment.

The maximal value of the fluid volumination is 1.050 in average after 24 hours, the antibody continuing to be present only for 3 days.

The highest fluid-serum volumination ratio is 0.96 after 24 hours and the highest number of leucocytes in the fluid is 1,100 after 24 hours (Table & Fig. 4.).

b) In case of the injection of 1/45 platinum loop of tetanus bacillus, the highest value of the volumination of the fluid is 1.034, the duration of the appearance of the antibody is for 6 days, the highest fluid-serum volumination ratio is 0.95 after 48 hours and the highest number of leucocytes in the fluid is 725 after 48 hours (Table & Fig. 5.).

c) After the injection of 1/15 platinum loop, the smallest lethal dose of tetanus bacillus, strain Riku. No. 3 (Table 6), the highest value of the volumi-

nation of the fluid is 1.024 after 24 hours, the antibody is demonstrable only for 3 days, the highest fluid-serum volumination ratio is 0.93 before the infection and 24 hours there after, the highest number of leucocytes in the fluid is 740 after 24 hours (Table 7 & Fig. 6).

d) When the same dose of tetanus bacillus, 1/15 platinum loop is injected and then tetanus-antiserum is given in the way above mentioned, the highest value of the volumination of the fluid is 1.024 after 24 hours, the duration of the appearance of the antibody in the

Table 6. Determination of lethal dose of tetanus bacillus in rabbits.

Number	Dose (p.l.)	Outcome of Animals
No. 8	1/300	alive
No. 9	1/300	〃
No. 20	1/60	〃
No. 21	1/60	〃
No. 22	1/60	〃
No. 23	1/60	〃
No. 28	1/45	〃
No. 29	1/45	〃
No. 31	1/45	〃
No. 32	1/45	〃
No. 13	1/30	〃
No. 19	1/15	dead
No. 18	1/15	〃
No. 17	1/15	〃
No. 16	1/15	〃
No. 12	1/6	〃
No. 11	2/3	〃
No. 10	5/3	〃

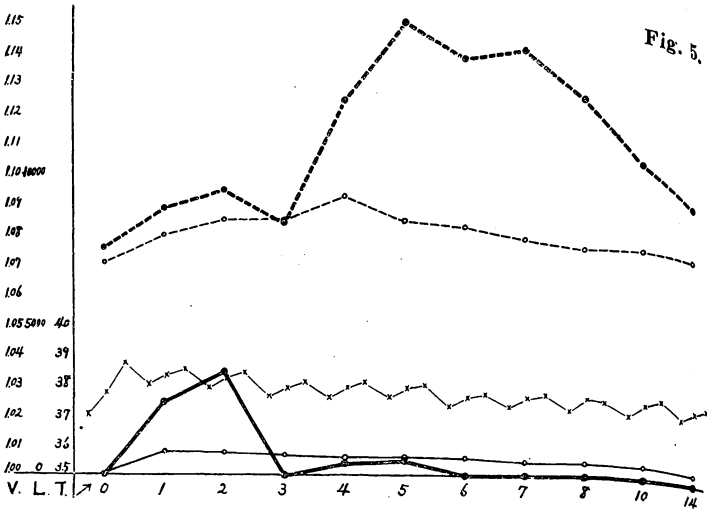


Fig. 5.

Table 5. Volumination of the fluid against tetanus bacillus in case of intracisternal injection of 1/45 platinum loop tetanus bacilli after preliminary anatoxin injection average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	19	7000	37.0	37.7	38.7	1.000	1.075	0.93
1	715	7900	38.0	38.3	38.5	1.024	1.088	0.94
2	725	8400	37.9	38.2	38.4	1.034	1.094	0.95
3	650	8400	37.6	37.9	38.1	1.000	1.083	0.92
4	605	9200	37.6	37.9	38.1	1.004	1.124	0.88
5	580	8400	37.6	37.9	38.0	1.005	1.150	0.87
6	575	8200	37.3	37.6	37.7	1.000	1.138	0.88
7	460	7800	37.3	37.6	37.7	1.000	1.141	0.88
8	460	7500	37.2	37.6	37.5	1.000	1.125	0.89
10	430	7600	37.1	37.5	37.7	1.000	1.105	0.90
14	345	7600	37.2	37.5	37.7	1.000	1.094	0.91

Table 7. Volumination of the fluid against tetanus bacillus in case of intracisternal injection of 1/15 platinum loop tetanus bacilli after preliminary anatoxin injection average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	21	6400	36.7	37.4	38.3	1.000	1.075	0.93
1	740	6800	37.8	38.2	38.3	1.024	1.104	0.93
2	735	7400	37.6	38.0	38.1	1.015	1.110	0.91
3	650	7600	37.5	37.8	37.9	1.000	1.091	0.92
4	655	7200	37.5	37.9	38.0	1.000	1.129	0.89
5	565	7800	37.3	37.7	37.9	1.000	1.150	0.87
6	525	7600	37.2	37.7	37.7	1.000	1.138	0.88
7	500	7500	37.1	37.5	37.4	1.000	1.137	0.88
8	460	7200	37.2	37.5	37.8	1.000	1.102	0.91
10	470	7200	37.2	37.6	37.6	1.000	1.100	0.91
14	370	7100	37.0	37.4	37.6	1.000	1.089	0.92

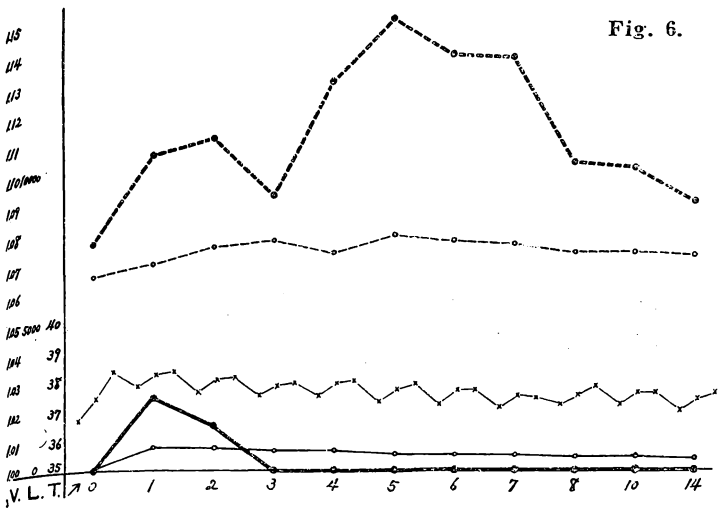


Fig. 6.

Table 8. Volumination of the fluid against tetanus bacillus in case of intracisternal injection of 1/15 platinum loop tetanus bacilli followed antiserum treatment average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	21	7000	37.1	37.6	39.0	1.000	1.073	0.93
1	715	7300	38.1	37.9	38.0	1.024	1.112	0.92
2	685	7700	37.9	38.1	38.4	1.009	1.110	0.91
3	620	7300	37.8	37.9	38.3	1.000	1.123	0.89
4	580	7300	37.5	37.8	38.1	1.000	1.125	0.89
5	495	7600	37.7	37.9	38.0	1.000	1.110	0.90
6	555	7500	37.5	37.8	38.0	1.000	1.108	0.90
7	575	7300	37.6	38.0	38.0	1.000	1.084	0.92
8	590	7400	37.4	37.7	37.9	1.000	1.098	0.91
10	550	7200	37.4	37.7	37.8	1.000	1.120	0.89
14	340	7300	37.3	37.6	37.8	1.000	1.099	0.91

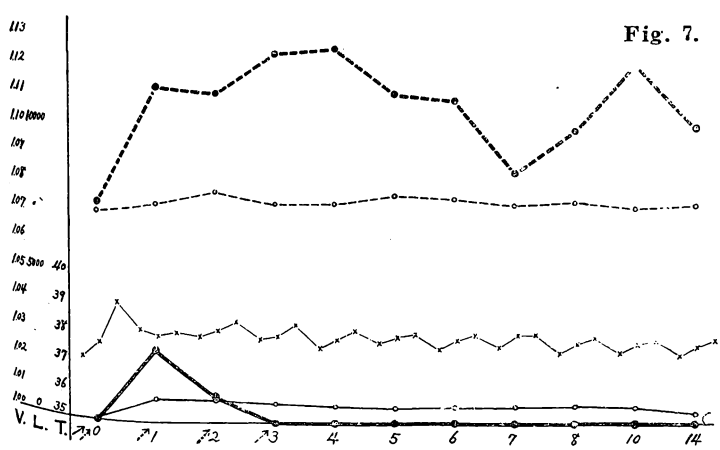


Fig. 7.

fluid is only for 3 days, the highest fluid-serum volumination ratio is 0.93 before the infection and the peak of the number of leucocytes in the fluid is 715 after 24 hours (Table 8 & Fig. 7).

Comment.

In meningitis of the rabbits, which have been preliminarily immunized, or which have been treated with antiserum after the infection, the duration of the demonstration of the antibody in the fluid is shorter than that in non-immunized rabbits [3 (6 in one) to 7 days].

The number of leucocytes in the fluid is larger in licopodium meningitis than in tetanal meningitis.

The highest fluid-serum volumination ratio seems to be smaller in immunized rabbits, a fact indicating that the volumination of the serum increases more remarkably than that of the fluid.

There are otherwise no remarkable differences between the two groups of animals in the experimental results.

3) Control experiment.

When tetanus-anatoxin

Fig. 8.

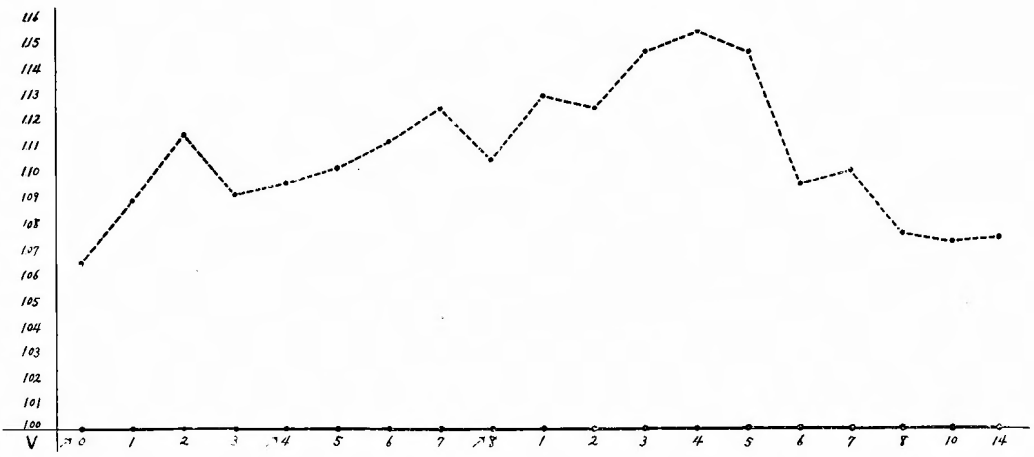


Fig. 9.

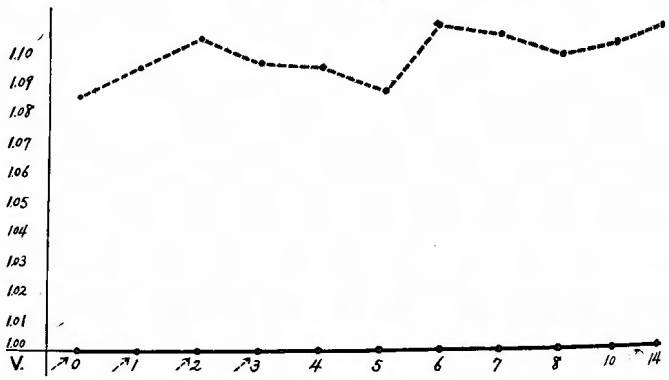


Table 9. Volumination of the fluid against tetanus bacillus following subcutaneous injection of anatoxin average of two rabbits.

Date	Fluid	Serum	Ratio
0	1.000	1.064	0.94
1	1.000	1.088	0.92
2	1.000	1.113	0.90
3	1.000	1.090	0.92
4	1.000	1.091	0.91
5	1.000	1.100	0.91
6	1.000	1.110	0.90
7	1.000	1.123	0.89
8	1.000	1.103	0.91
1	1.000	1.128	0.89
2	1.000	1.123	0.89
3	1.000	1.115	0.87
4	1.000	1.153	0.87
5	1.000	1.145	0.87
6	1.000	1.094	0.91
7	1.000	1.099	0.91
8	1.000	1.075	0.93
10	1.000	1.072	0.93
14	1.000	1.071	0.93

Table 10. Volumination of the fluid against tetanus bacillus following the administration of antiserum average of two rabbits.

Date	Fluid	Serum	Ratio
0	1.000	1.085	0.92
1	1.000	1.095	0.91
2	1.000	1.105	0.90
3	1.000	1.097	0.91
4	1.000	1.095	0.91
5	1.000	1.085	0.92
6	1.000	1.105	0.90
7	1.000	1.099	0.91
8	1.000	1.089	0.92
10	1.000	1.090	0.92
14	1.000	1.093	0.91

or antiserum only has been introduced subcutaneously, no trace of the volumination is demonstrable in the fluid (Table 9, 10 & Fig. 8, 9).

Ⅳ. Changes in the amount of antibodies appearing in the cerebrospinal fluid in pneumococcus meningitis.

Table 11. Volumination of the fluid against pneumococcus in case of meningitis caused by intracisternal injection of 1/400,000 platinum loop pneumococci average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	22	6900	37.3	37.8	38.7	1.000	1.048	0.95
1	535	7200	37.0	38.2	38.5	1.050	1.078	0.98
2	550	7600	37.6	38.8	38.7	1.050	1.080	0.97
3	490	7600	37.9	38.7	38.8	1.045	1.080	0.97
4	600	9500	38.3	38.6	38.6	1.031	1.099	0.94
5	800	10300	37.5	38.0	38.4	1.005	1.095	0.92
6	950	12000	38.4	38.3	38.5	1.010	1.084	0.93
7	800	7900	37.5	38.2	38.2	1.000	1.073	0.93
8	830	8000	37.1	38.0	38.1	1.000	1.084	0.92
10	510	8300	36.6	37.4	37.7	1.000	1.073	0.93
14	420	6900	36.4	36.7	36.8	1.000	1.064	0.94

Fig. 10.

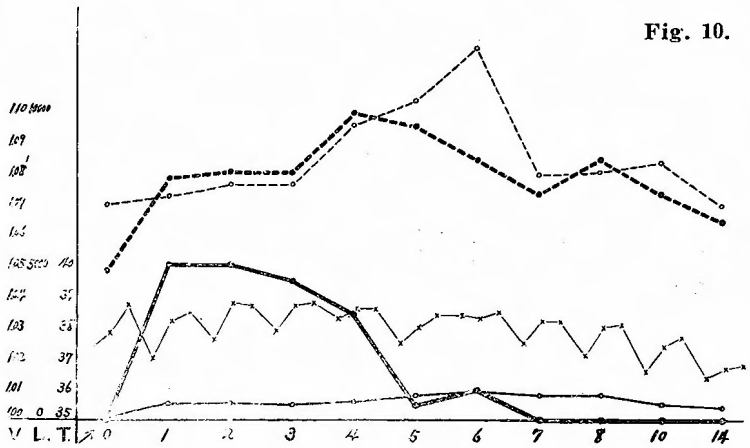


Table 12. Volumination of the fluid against pneumococcus in case of meningitis caused by 1/200,000 platinum loop pneumococci average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	20	6300	37.0	37.5	38.1	1.000	1.043	0.96
1	995	6600	37.7	38.1	38.6	1.058	1.078	0.98
2	725	7900	38.0	38.1	38.3	1.065	1.095	0.97
3	850	7500	37.6	38.4	38.7	1.035	1.090	0.95
4	640	8300	38.5	38.8	38.8	1.039	1.091	0.95
5	560	9000	37.9	38.8	39.6	1.015	1.080	0.94
6	760	8300	37.8	38.2	38.3	1.005	1.078	0.94
7	610	6700	37.7	38.2	38.8	1.000	1.069	0.94
8	715	7300	36.6	37.3	37.5	1.000	1.084	0.92
10	160	6300	36.4	36.8	37.0	1.000	1.073	0.93
14	250	6250	36.3	36.6	36.9	1.000	1.051	0.95

1) Experiments in the normal rabbits.

a) When 1/400,000 platinum loop of pneumococcus has been introduced into the meningeal space, the highest value of the volumination of the fluid against pneumococcus is 1.050 after 24 and 48 hours, the duration of the volumination of the fluid is for 7 days, the highest fluid-serum volumination ratio is 0.98 after 24 hours and the peak of the pleocytosis is 950 after 6 days (Table 11 & Fig. 10).

b) In case of 1/200,000 platinum loop, the highest value of the volumination of the fluid is 1.065 after 48 hours, the persistence of the fluid volumination is for 7 days, the highest fluid-serum volumination ratio is 0.98 after 24 hours and the peak of the pleocytosis is 995 after 24 hours (Table 12 & Fig. 11).

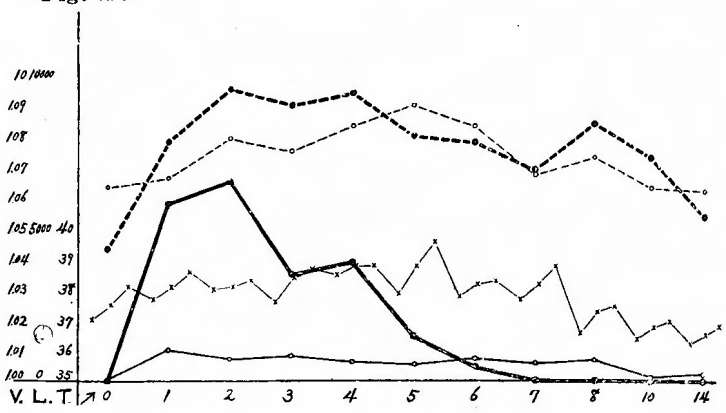
Comment.

The occurence and duration of the volumination of the fluid in pneumococcus meningitis are almost the same as those in tetanus meningitis.

However, the highest fluid-serum volumination

ratio is higher in the former. The body temperature of the rabbits rises for about one week, but the increase in the fluid leucocytes does not much differ from that in tetanus meningitis.

Fig. 11.



2) Experiments in the rabbits, preliminarily immunized.

a) When 1/2,000 platinum loop of pneumococcus, more than the lethal dose of pneumococcus, strain No. 2 (Table 13), has been introduced intracisternally, the highest average value of the fluid volumination against pneumococcus is 1.045 after 48 hours, the persistence of the volumination of the fluid is only for 4 days, the highest fluid-serum volumination ratio is 0.96 after 24 – 48 hours and the peak of the pleocytosis is 860 after 24 hours (Table 14 & Fig. 12).

Table 14. Volumination of the fluid against pneumococcus in case of meningitis due to 1/2,000 platinum loop pneumococci average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	10	6200	36.2	36.8	37.6	1.000	1.049	0.95
1	860	7700	36.8	37.8	38.0	1.024	1.064	0.96
2	800	7100	37.0	37.5	38.2	1.045	1.085	0.96
3	435	7000	37.5	38.3	38.5	1.009	1.074	0.94
4	390	7300	37.4	38.2	38.5	1.000	1.058	0.95
5	605	6900	37.4	38.0	38.5	1.000	1.062	0.94
6	245	7200	37.2	38.0	38.2	1.000	1.064	0.94
7	225	6900	37.5	38.7	38.8	1.000	1.066	0.94
8	190	7000	37.2	37.7	38.0	1.000	1.051	0.95
10	195	6850	36.8	37.2	37.6	1.000	1.059	0.94
14	205	6800	36.5	36.9	37.2	1.000	1.053	0.95

Fig. 12.

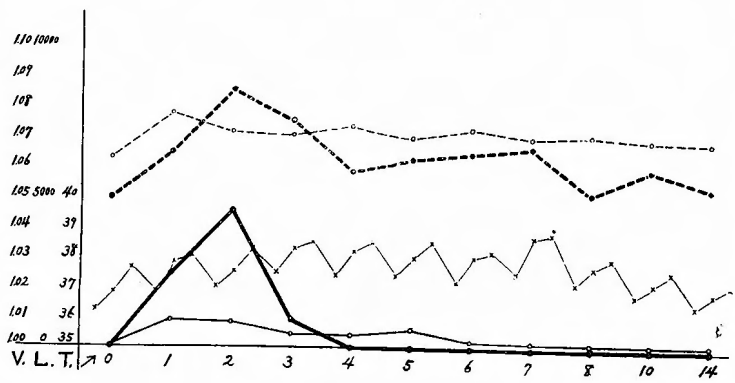


Table 13. Determination of lethal dose of pneumococcus in rabbits.

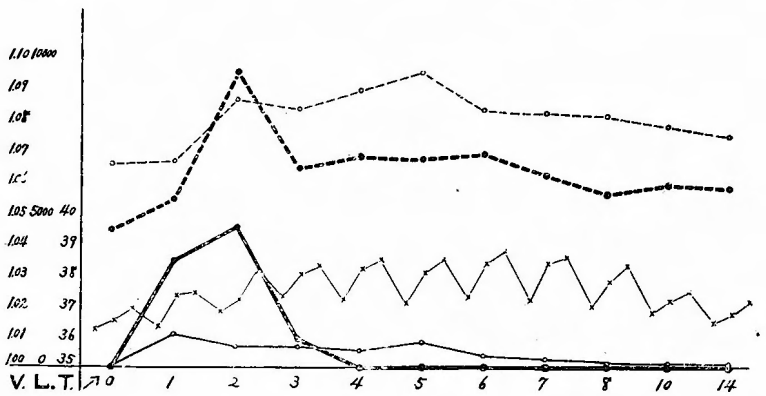
Number	Dose (p.l.)	Outcome of Animals
No. 96	1/1,000,000	alive
No. 108	1/400,000	〃
No. 109	1/400,000	〃
No. 106	1/200,000	〃
No. 107	1/200,000	〃
No. 95	1/100,000	〃
No. 104	1/80,000	dead
No. 103	1/80,000	〃
No. 102	1/40,000	〃
No. 101	1/40,000	〃
No. 94	1/10,000	〃
No. 100	1/6,000	〃
No. 99	1/4,000	〃
No. 98	1/2,500	〃
No. 97	1/1,500	〃
No. 93	1/1,000	〃
No. 92	1/100	〃

b) When 1/1,000 platinum loop of pneumococcus has been introduced into the meningeal space, the highest average value of the fluid volumination is 1.045 after 48 hours the persistence of the volumination of the fluid is only for 4 days, the highest fluid-serum volumination ratio is 0.98 after 24 hours and the peak of the pleocytosisis is 1,040 after 24 hours (Table 15 & Fig. 13).

Table 15. Volumination of the fluid against pneumococcus in case of meningitis caused by 1/1,000 platinum loop pneumococci average of two rabbits.

Date	Leucocytes		Temperature			Volumination		Ratio
	Fluid	Blood				Fluid	Serum	
0	15	6500	36.2	36.5	36.9	1.000	1.011	0.92
1	1040	6600	36.3	37.3	37.4	1.034	1.051	0.98
2	665	8600	36.8	37.2	38.1	1.045	1.095	0.95
3	640	8300	37.3	38.0	38.3	1.009	1.061	0.95
4	550	8900	37.2	38.2	38.5	1.000	1.068	0.93
5	795	9500	37.1	38.2	38.5	1.000	1.067	0.94
6	370	8300	37.3	38.4	38.8	1.000	1.069	0.94
7	285	8200	37.2	38.4	38.6	1.000	1.062	0.94
8	180	8100	37.0	37.8	38.3	1.000	1.056	0.95
10	175	7800	36.8	37.2	37.5	1.000	1.059	0.94
14	180	7500	36.5	36.8	37.2	1.000	1.058	0.95

Fig. 13.



Comment.

In the immunized rabbits, the duration of the appearance of the volumination of the fluid is much shorter than that in the non-immunized ones (4 to 7 days). The highest fluid-serum volumination ratio and the highest average value of the volumination of the fluid seem to be lower in the former group.

The body temperature of the rabbits does not show a recognizable difference between the immunized and the non-immunized animal groups ; i. e. it continues to rise for about a week in both groups. The increase in leucocytes in the cerebrospinal fluid does not reach such a high level in pneumococcus meningitis as the peak in licopodium meningitis.

Discussion and summary.

1) The number of leucocytes in the cerebrospinal fluid has increased to a higher level in licopodium meningitis.

2) If preventive or therapeutic immunological procedures have been made before or after the infection, the highest fluid-serum volumination ratio tends to become lower. The reason seems to be in the facts that in meningitis of the animals thus treated, the volumination of the serum tends to increase to a higher level than in meningitis of untreated ones, whereas the volumination of the fluid

does not increase correspondingly.

3) Meningitis never fails to occur, even if preventive immunological procedures have been made subcutaneously or intracutaneously about a week or two before the infection. But the course of meningitis becomes much shorter and more simple.

4) Almost the same effect is obtained when the tetanus-antiserum has been given shortly after the infection.

5) Body temperature of the rabbits does not essentially rise both in case of licopodium and in tetanus meningitides, but definitely rises for about one week in pneumococcus meningitis, even in case of preliminarily immunized ones.

6) No antibodies can be demonstrated in the cerebrospinal fluid by means of volumination either in the normal rabbits or in those which have been immunized subcutaneously by tetanus-anatoxin or antiserum, unless their meninges become infected. Antibodies appear in the fluid only when septic or aseptic meningitis takes place.

7) It has not been determined in the experiments here, whether the anti bodies in the fluid are specific for tetanus bacillus, or for pneumococcus, or not. However, they may be specific in some of the experiments and unspecific in others, judging from common serological principles.

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和文抄錄

実驗的髄膜炎に於ける髄液特殊或いは非特殊免疫抗体

京都大学医学部外科学第一講座（荒木教授）
大学院学生 鷲 見 洋

先に教室に於て加藤が行つた，急性化膿性髄膜炎に於ける髄液内抗体の変化に関する実験の続篇として，

私は抗体産生の顕著であると考えられる破傷風菌（陸3株）及び肺炎双球菌（2型）を用いて，実験的髄膜炎を起した場合の髄液増容反応を検し，次の如き結果を得た．

1) 破傷風菌感染及び Licopodium 後頭下注入の場合は，著明な体温上昇は認められないが，肺炎双球菌感染に際しては，一週間余りの軽度の発熱が認められる．後者は免疫処置に依つて著明な影響を受ける様には想われない．然しこの際感染に用いられた菌量に差異がある事は考慮に入れられなければならないだろう．

2) 髄液白血球数は単なる異物であるる Licopodium に依る無菌性髄膜炎に於て最高の値を示して居り，破傷風菌，肺炎双球菌共に Licopodium 以上の滲出は起さない．特に破傷風菌に於ては肺炎双球菌及び加藤の行つた葡萄状球菌．大腸菌に比べ遙に多量の1/45又は1/15白金耳の菌量を注入しても，左程著明な滲出を見ないのは，之が Licopodium と同様に単なる異物としての働きのみしか示して居ないと考える根拠となるであろう．即破傷風菌は髄液腔に於ては一種の雑菌に過ぎないと考えたい．

3) 髄液増容反応は Licopodium，破傷風菌，肺炎双球菌三者共略一週間継続するが，免疫前処置を施した場合には髄膜炎は起るが，その経過は著明に短縮される．又対血清増容反応比率も低下する傾向が見られる．

又感染の直後から破傷風抗血清を用いても結果は略同様である．

4) 正常家兎の髄液は増容反応を起さない．更に，破傷風アナトキシン又は抗血清，肺炎双球菌ワクチンを皮下或は皮内に注射しただけでは髄液の増容反応は起らず，髄液増容反応が起るのは髄膜炎を起した場合に限る事は明らかである．

本誌7月号予告

綜説

原著

症例報告